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EXAMINER

CHONG, KIMBERLY

ART UNIT PAPER NUMBER

1635

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/994,412

Applicant(s)

CERTA ET AL.

Examiner

Kimberly Chong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 06/22/2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Status of the Application***

Claims 1-6 are pending and currently under examination. Claims 7 and 8 are withdrawn.

### ***Claim Rejections - 35 USC § 112***

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a process for inhibiting expression of a target gene in cells or tissue in vitro, comprising infecting cells or tissues with viral particles consisting essentially of ssRNA which expresses a sense RNA strand and viral particles consisting essentially of ssRNA which expresses an anti-sense RNA strand.

It is unclear if the cells or tissues are infected with viral particles consisting of a sense *and* antisense RNA strands in the same viral particles or if the cells or tissues are infected with a first set of viral particles consisting of a sense RNA strand and also infected with a second set of viral particles consisting of an antisense RNA strand.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Ding et al. (Nucleic Acids Research, 1998).

The instant claims are drawn to a process for inhibiting expression of a target gene from a cell or tissue by administration of viral particles expressing a sense RNA strand and an antisense RNA strand targeted to a cell or tissue. Further the claims recite the cell or tissue is infected with equal amounts of viral particles consisting of sense ssRNA and antisense ssRNA. The claims further recite the target gene is eukaryotic, viral or synthetic and the homologous nucleotide sequence is at least 50 bases in length and is specific for a target gene.

Ding et al. teach a process for inhibiting expression of a viral gene in cells or tissues, *in vitro*, by administration of viral particles comprising a sense ssRNA or an antisense ssRNA targeted to viral genes (see page 3271, materials and methods). Ding et al. teach the cells are infected with equal amounts of viral particles (see page 3272, second column, first paragraph). Ding et al. further teach the ribonucleic acid sequences are at least 50 bases in length (see Figure 1).

Thus, Ding et al. anticipates claims 1, 2, 4 and 6 of the instant application.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding et al. (Nucleic Acids Research, 1998) in view of Lundstrom K. (J. Receptor and Signal Transduction, 1999).

The instant claims are drawn to a process for inhibiting expression of a target gene from a cell or tissue by administration of viral particles expressing a sense RNA strand and an antisense RNA strand targeted to a cell or tissue. Further the claims recite the cell or tissue is infected with equal amounts of viral particles consisting of sense ssRNA and antisense ssRNA. The claims further recite the RNA is cloned into an alphavirus and the target gene is eukaryotic, viral or synthetic and the homologous nucleotide sequence is at least 50 bases in length and is specific for a target gene.

Ding et al. teach a process for inhibiting expression of a viral gene in cells or tissues, *in vitro*, by administration of viral particles comprising a sense ssRNA or an antisense ssRNA targeted to viral genes (see page 3271, materials and methods). Ding et al. teach the cells are infected with equal amounts of viral particles (see page 3272, second column, first paragraph). Ding et al. further teach the ribonucleic acid sequences are at least 50 bases in length (see Figure 1). Ding et al. does not teach the viral vector is an alphavirus.

Lundstrom teach alphavirus vectors, such as Semliki Forest Virus vectors, for production of high titer viral particles (see page 680).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the viral vector, as taught by Ding et al., with an alphavirus vector, as taught by Lundstrom.

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One would have been motivated to substitute the viral vector in Ding et al. with an alphavirus vector because Lundstrom specifically teach alphavirus are known for their extremely broad host range and the ability to produce high titer viral particles make them favorable for gene therapy applications (see page 680).

Finally, one would have a reasonable expectation of success because Lundstrom teach production of alphavirus particles and use in gene transfer into cells. Further Lundstrom teach an efficient high titer alphavirus viral particle packaging system.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-2 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding et al. (Nucleic Acids Research, 1998) in view of Fire et al. (see form PTO-892, US Patent Documents #A).

The instant claims are drawn to a process for inhibiting expression of any target gene from any cell or tissue by administration of viral particles expressing a sense RNA strand and an antisense RNA strand targeted to any cell or tissue. Further the claims recite the ssRNA strand is cloned into a viral vector wherein equal amounts of viral particles containing sense and antisense

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ssRNA. The claims further recite the target gene is eukaryotic, viral or synthetic and the homologous nucleotide sequence is at least 50 bases in length and is specific for a target gene. Additionally, the claims recite the target gene is a developmental gene, an oncogene, a tumor suppressor gene or an enzyme.

Ding et al. teach a process for inhibiting expression of a viral gene in cells or tissues, *in vitro*, by administration of viral particles comprising a sense ssRNA or an antisense ssRNA targeted to viral genes (see page 3271, materials and methods). Ding et al. teach the cells are infected with equal amounts of viral particles (see page 3272, second column, first paragraph). Ding et al. further teach the ribonucleic acid sequences are at least 50 bases in length (see Figure 1). Ding et al. does not teach targeted a developmental gene, an oncogene, a tumor suppressor gene or an enzyme.

Fire et al. teach a process for inhibiting expression of a target gene in cells or tissues (see column 6, lines 32-45) by administration of a RNA wherein the RNA strands comprise homologous nucleotide sequences to a portion of the said target gene (see column 7, lines 53-68). Fire et al. further teach double stranded structures can be formed by two complementary RNA strands inside the cell (see column 7, lines 42-53). Further, Fire et al. teach the RNA can be introduced into a cell by a viral construct packed into a viral particle (see column 9, lines 49-55). Additionally, Fire et al. teach the length of the homologous nucleotide sequence is at least 50 bases (see column 8, lines 1-5). Fire et al. further teach the target gene may be eukaryotic, viral or synthetic (see column 8, lines 12-63) and the target gene may be a developmental gene, an oncogene, a tumor suppressor gene or an enzyme (see column 11, lines 8-37).

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to target a developmental gene, an oncogene, a tumor suppressor gene or an enzyme, as taught by Fire et al. by infecting cells or tissues with viral particles consisting of RNA, as taught by Ding et al.

One would have been motivated to target a developmental gene, an oncogene, a tumor suppressor gene or an enzyme because Fire et al. teach targeting the above listed genes and a process of inhibiting gene expression from the disclosed target genes (see columns 7 and 8) and further targeting specific genes is an approach for drug target validation and gene function discovery.

Finally, one would have a reasonable expectation of success of targeting a developmental gene, an oncogene, a tumor suppressor gene or an enzyme given that Fire et al. teach design of a sense and antisense compound targeted to a gene listed above and further teach screening sense and antisense RNA capable of forming a dsRNA that effectively inhibit gene expression.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

### ***Response to Applicant's Arguments***

#### ***Claim Rejections - 35 USC § 112***

The rejection of record of claims 1-6 under 35 U.S.C. 112, first paragraph, lack of enablement is withdrawn in response to Applicant's arguments filed 06/20/2005.



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The rejection of record of claims 2 and 3 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in response to Applicant's arguments filed 06/22/2005.

***Claim Rejections - 35 USC § 102***

The rejection of record of 1-2 and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Fire et al. (U.S. Patent Number 6,506,559) is withdrawn in response to Applicant's arguments filed 1/19/2005.

***Claim Rejections - 35 USC § 103***

The rejection of record of claims 1-4, 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (U.S. Patent Number 6,506,559), in view of Johanning et al. (Nucleic Acids Research 1995, Vol.23 (9): 1495-1501) is withdrawn in response to Applicant's arguments filed 1/19/2005.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. **Please note the**


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**Central FAX number has been changed. Faxes send to the old number (703-872-9306) will be routed to the new number until September 15, 2005.**

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Kimberly Chong  
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